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RESONANCE PHENOMENA IN CELL POPULATION CHEMOTHERAPY MODELS

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1. Introduction. Mathematical models of cell population dynamics offer a means to predict the effectiveness of chemotherapy treatments. The basic ideas of such models are to view chemotherapy as a loss function for both normal and tumor cell populations, and to design optimal treatment regimens in consideration of the parameters that distinguish normal and tumor cells.

In this paper we will focus upon the qualitative analysis of periodic chemotherapy applications. For this purpose we use an age- and size-structured model of cell population dynamics with a time periodic loss function. The normal and tumor cell populations have the same model but with different parameters. The main difference of the two populations is the longer mean cycle length of tumor cells. This difference results in a remarkable resonance effect in the presence of periodic phase-specific cell loss. A marked preferential advantage for the normal cell population occurs when the treatment period is close to the mean cycle length of normal cells. This resonance effect is apparent through a wide range of age- and size-dependent parameter values. It is evident whenever a phase-sensitive loss is impressed upon two age-structured proliferating cell populations with distinct mean division-age frequencies. This resonance phenomenon was discovered by Dibrov et al. [**13**], who studied it from a numerical point of view with age-structured models of cell population dynamics. A similar selective synchrony effect was studied by Rotenberg [**31**]. In this paper we will present examples to demonstrate that resonance phenomena are present in more refined cell population models. The general age- and size-structured model we use includes the well-known transition probability, size control, and inherited properties models of cell population dynamics. It also allows for the asymmetric division of mother cells, which some researchers believe to be a primary explanation of cell cycle variability (M. Kimmel et al. [**22**]). The use of a size-structure variable also allows a more accurate

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